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OPERATED BY
CARBIDE AND CARBON CHEMICALS COMPANY
A DIVISION OF UNION CARBIDE AND CARBON CORPORATION
UCC
POST OFFICE BOX P
OAK RIDGE, TENN.

January 23, 1956

Dear Josh,

Naturally I have had in mind for many years a comprehensive screening of agents for mutagenic and/or dominant nuclear lethal effects by using the heterokaryon methods, but have not gotten around to it. The only definite information I have is as follows: Nitrogen mustard gives the expected radiomimetic effects; heating, aging, and compressed oxygen had non-nuclear killing effects and did not increase recessive lethals within experiments involving ca. 500 isolates; stilbamidine and pentamidine were extremely toxic, but showed non-nuclear killing and no increase in recessive lethals in ca. 100 isolates. Manganous chloride had no detectable effects, perhaps because the conidia were not preconditioned. If it will help you a great deal, I will undertake testing of the agents in which you are most interested, and could easily screen 50 compounds per month for dominant nuclear effect in spare time. If recessive lethal data are needed I would have to devote full time to the problem, which I am unwilling to do.

The two main reasons for not beginning this work until now have been, first, I have not yet published a satisfactory account of the theory of the analysis, and second, the homology test methods have not been sufficiently streamlined to permit a large scale analysis of the recessive mutations for preferential effects of different agents, the real point of interest from my standpoint. I am preparing a manuscript now for the Winge memorial issue of the Comptes Rendues of the Carlsberg Laboratories, with the provisional title "Dominant nuclear lethal mutation in Neurospora". This will solve the first problem, since the deadline is only a month away. I hope you will consent to going over this paper carefully and giving your criticisms; this would be a great help to me, since I am suffering from loss of perspective.

At present the machine shop is making a simple grid device which will place homology tests on a semiautomatic basis. The first use I plan for this is an exhaustive analysis of temperature sensitive mutations. If my hunch is correct that these are members of a selected class only about twice as large as the reparable class, they should number around 500, and only 124,750 homology tests would catch all but 1/e of them.

I have not yet heard from Bowers, but will certainly follow up immediately if he writes. I am not yet ready with any detailed plans or suggestions which go further than your outline, but am making it a point to step off the treadmill at regular intervals to give some thought to the matter.

My best to you and Esther,

Kim